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Cross-sectional analysis of educational inequalities in primary prevention statin use in UK Biobank

Alice R Carter, PhD [1,2*], Dipender Gill, BMBCh PhD [3-7], George Davey Smith, FRS [1,2,8], Amy E Taylor, PhD [2,8], Neil M Davies, PhD, [1,2,9†], Laura D Howe, PhD [1,2†]

1) MRC Integrative Epidemiology Unit, University of Bristol
2) Population Health Sciences, Bristol Medical School, University of Bristol
3) Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
4) Centre for Pharmacology & Therapeutics, Department of Medicine, Hammersmith Campus, Imperial College London, London, UK.
5) Novo Nordisk Research Centre Oxford, Old Road Campus, Oxford, UK
6) Clinical Pharmacology and Therapeutics Section, Institute of Medical and Biomedical Education and Institute for Infection and Immunity, St George's, University of London, London, UK
7) Clinical Pharmacology Group, Pharmacy and Medicines Directorate, St George's University Hospitals NHS Foundation Trust, London, UK
8) NIHR Bristol Biomedical Research Centre, University of Bristol
9) K.G. Jebsen Center for Genetic Epidemiology, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Norway.

[†]NMD and LDH contributed equally

Corresponding author:

Dr Alice R Carter

Oakfield House,

Oakfield Grove,

Bristol,

BS8 2BN

alice.carter@bristol.ac.uk

@alicerosecarter

ORCiD: 0000-0003-2817-4195

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Abstract

Objective:

Identify whether participants with lower education are less likely to report taking statins for primary cardiovascular prevention than those with higher education, but an equivalent increase in underlying cardiovascular risk.

Methods:

Using data from a large prospective cohort study, UK Biobank, we calculated a QRISK3 cardiovascular risk score for 472 097 eligible participants with complete data on self-reported educational attainment and statin use (55% female; mean age, 56). We used logistic regression to explore the association between i) QRISK3 score and ii) educational attainment on self-report statin use. We then stratified the association between QRISK3 score and statin use, by educational attainment to test for interactions.

Results:

There was evidence of an interaction between QRISK3 score and educational attainment. Per unit increase in QRISK3 score, more educated individuals were more likely to report taking statins. In women with ≤7 years of schooling, a one unit increase in QRISK3 score was associated with a 7% higher odds of statin use (odds ratio (OR)(1.07, 95% CI 1.07, 1.07). In women with ≥20 years of schooling, a one unit increase in QRISK3 score was associated with an 14% higher odds of statin use (OR 1.14, 95% CI 1.14, 1.15). Comparable ORs in men were 1.04 (95% CI 1.04, 1.05) for ≤7 years of schooling and 1.08 (95% CI 1.08, 1.08) for ≥20 years of schooling.

Conclusion:

Per unit increase in QRISK3 score, individuals with lower educational attainment were less likely to report using statins, likely contributing to health inequalities.

Summary

What is already known on this topic?

Despite reductions in the rates of cardiovascular disease in high income countries, individuals who are the most socioeconomically deprived remain at the highest risk of disease. Although intermediate lifestyle and behavioural risk factors explain some of this, much of the effect remains unexplained.

What does this study add?

Per unit increase in QRISK3 score, a measure of clinical need, the likelihood of statin use increased more in individuals with high educational attainment compared with individuals with lower educational attainment .These results were similar when using UK Biobank to derive QRISK3 scores and when using QRISK scores recorded in primary care records, and when using self-reported statin prescription data or prescription data from primary care records.

How might this impact clinical practice?

The mechanisms leading to these differences are unknown, but both health seeking behaviours and clinical factors may contribute. Clinicians and policy makers should consider how they can improve uptake of preventative health checks to carry out risk cardiovascular risk assessments, whilst also considering whether any clinic level factors could be addressed to improve the uptake of statins in lower educated patients.

Introduction

Despite reductions in cardiovascular disease (CVD) morbidity and mortality in high-income countries, the most socioeconomically deprived groups have the highest risk of disease (1). There is evidence that education is a causal risk factor for CVD (2).

Previous studies have assessed the association of socioeconomic position (SEP) with primary and secondary treatment rates for statins with mixed results (3-8). Lower education is associated with higher levels of cardiovascular risk factors (2) and therefore a greater underlying cardiovascular risk and clinical need for statins. However, educational differences in health-seeking behaviours or interactions between patients and clinicians, may mean higher educated patients are more likely to be prescribed statin medication (9). Independent of SEP, an over-use of statins in patients at low cardiovascular risk and under-use of statins in patients at high cardiovascular risk has been reported (8, 10).

Using UK Biobank, we investigated whether for a unit increase in QRISK3 cardiovascular risk score (11), participants with lower education were less likely to report taking statins for primary prevention than those with higher education. At the time of data collection (2006-2010) guidelines recommended prescribing statins to individuals with a ≥20% risk of experiencing an adverse cardiac event in 10 years, calculated using the Framingham risk score (12). In England and Wales, these guidelines have been updated to recommend prescribing based on a QRISK3 score of ≥10% (13). Cardiovascular risk assessments are typically carried out by a primary healthcare professional during routine health checks . Since 2004, low-dose statins have also been available to purchase over the counter from a pharmacy.

Methods

UK Biobank

At baseline, UK Biobank recruited 503 317 UK adults, aged 37 to 73 years, from 2006-2010. Participants attended assessment centres involving questionnaires, interviews, anthropometric and physical measurements (14). This analysis uses data from baseline assessments, linked hospital inpatient records and mortality statistics and linked primary care data (including prescriptions). Ethical approval for this study was sought from UK Biobank (project 10953).

QRISK score

Cardiovascular risk was assessed using the publicly available QRISK3 algorithm (see https://qrisk.org/three/index.php) (11). QRISK3 scores were derived for all participants with complete data on education, self-reported statin use and with no prevalent CVD (see exclusion criteria) (N= 472 097) (Figure 1). Multiple imputation was used for missing data in the QRISK3 variables (see statistical analysis section).

See Supplementary Methods and Supplementary Table 1 for full details of all QRISK3 variables and Supplementary Tables 2 and 3 for UK Biobank treatment codes, ICD-9 and ICD-10 codes used to define diagnoses .

In a subset of individuals with linked primary care data, QRISK (read 2 code: 38DF.) (N=1 495), and QRISK2 scores (read 2 code: 39DP.) (N = 10 633) were recorded from 2007 onwards. In sensitivity analyses, the first recorded QRISK score was used.

Measuring education

Self-reported highest qualification was converted to the International Standard Classification for Education (ISCED) for years of education (Supplementary Table 4).

Measuring statin use

Regularly prescribed medication was reported to study nurses, which was used define i) statin use and ii) type of statin used (Atorvastatin, Simvastatin, Fluvastatin, Pravastatin and Rosuvastatin).

In individuals with primary care data, self-report statin use was validated by a statin prescription both 3 months before and 3 months after baseline. In sensitivity analyses using primary care QRISK scores, statin use was defined as any statin prescription after a QRISK score was recorded, excluding individuals who reported using statins at baseline.

Exclusion criteria

Individuals were excluded if they had at least one diagnosis of myocardial infarction, angina, stroke, transient ischaemic attack, peripheral arterial disease, type 1 diabetes, chronic kidney disease or familial hypercholesterolaemia at baseline, as NICE guidelines state these diagnoses should result in a statin prescription (13), defined using ICD codes in hospital inpatient data (Supplementary Table 3).

Complete case analyses were carried out on 368 721 individuals, with complete data on age, sex, education, self-reported statin use and all QRISK3 variables (Supplementary Table 1 and Figure 1).

Code and data availability

The derived variables have been returned to UK Biobank. The code used to derive QRISK3 scores, and conduct analyses is available at github.com/alicerosecarter/statin_inequalities. All analyses were carried out in Stata version 16.1 (StataCorp, College Station, Texas 77845 USA).

Statistical analyses

To maximise power and potentially reduce bias, multivariable multiple imputation by chained equations (15) was used to impute missing data in QRISK3 variables, assuming missing at random. The imputation sample was defined as all individuals with complete data on education and reported statin use. The

proportion of missing data for each variable ranged from 0% to 15% (Supplementary Table 5). Imputation was carried out within strata of education and sex to preserve interactions (16). A total of 25 imputed datasets were generated (17), each analysed individually with results combined according to Rubin's rules.

Because the QRISK3 score is derived sex-stratified, analyses were carried out sex stratified (11).

To confirm the validity of the derived QRISK3 score, a univariable logistic regression model was used to assess the association between QRISK3 score and i) statin use (as defined previously) and ii) incident CVD (see Supplementary Methods).

We estimated the association between years of education with i) QRISK3 score (using linear regression) and ii) statin use (using logistic regression).

Testing for interaction between QRISK3 score and education on statin use

Logistic regression was used to estimate the association of QRISK3 score with statin use, stratified by years of education, estimating multiplicative interactions (sFigure 2, Route 1). Analyses were adjusted for date of assessment to account for changes in statin prescribing guidelines during the recruitment period. No other covariates were adjusted for, assuming all relevant variables are incorporated into the QRISK3 score. Evidence of an interaction between QRISK3 score and years of education was evaluated in a linear model where the interaction term QRISK3×education was included.

Secondary analyses

Atorvastatin has greater efficacy than Simvastatin but is more costly (18). To test whether educational inequalities are present in the statin type prescribed, we estimated the interaction between QRISK3×education with Atorvastatin compared with Simvastatin in statin users (sFigure 1 Route 2).

Analyses between QRISK3×education on statin use and type of statin were replicated using complete case data (sFigure 1, Route 3 and 4).

Analyses were replicated in participants with linked primary care data using i) baseline measures of QRISK3 and self-report statin use (sFigure 1, Route 5) ii) baseline measures of QRISK3 with validated statin use (sFigure 1, Route 6) and iii) QRISK or QRISK2 score recorded in primary care data with statin prescriptions (sFigure 1, Route 7). Primary care QRISK scores were included if they were recorded on or prior to the date of first statin prescription, but time between both events was not accounted for.

Sensitivity analyses were carried out excluding participants who reported taking non-statin lipid-lowering therapies. Main analyses were also replicated on the additive scale for interaction.

Two further QRISK3 scores were derived using baseline data excluding i) systolic blood pressure variability and ii) family history of CVD from QRISK3 scores (see supplementary methods). The pairwise correlation between scores with and without these variables was tested.

Results

UK Biobank sample

In primary analyses (N = 472 097) 55% of participants were female with a mean age of 56. In females, the QRISK3 score implied a mean 10-year risk of a cardiovascular event of 6.9% (standard deviation (SD) = 5.5). In males, the QRISK3 score implied mean a 10-year risk of a cardiovascular event of 13.1% (SD = 8.4). Participants were more likely to have completed ≥20 years of education (female = 35%, male = 38%) than ≤7 years of education (female = 14%, male = 14%). 10% of females and 17% of males reported using statins (Supplementary Table 6).

The distribution of variables was similar between the multiply imputed data, complete case data, and the subset of participants with primary care data (Supplementary Table 6).

Association of QRISK3 score with statins and cardiovascular disease

Per one unit increase in QRISK3 score (i.e., a 1% increase in the 10-year risk of experiencing a cardiovascular event) in females, the odds ratio (OR) for statin use was 1.12 (95% confidence interval [CI]: 1.12 to 1.13) and the OR for incident CVD was 1.14 (95% CI: 1.14 to 1.15) (Figure 2, Supplementary Figure 2 and Supplementary Table 7). Females with a QRISK3 score of ≥10 were 1.34 times (95% CI: 1.31 to 1.36) more likely to report using statins than those with a QRISK score <10. In males, the OR for statin use was 1.07 (95% CI: 1.07 to 1.07) and 1.09 (95% CI: 1.09 to 1.09) for incident CVD per unit higher QRISK3 score (Figure 2, Supplementary Figure 2 and Supplementary Table 7). Males with a QRISK3 score of ≥10 were 1.49 times (95% CI: 1.46 to 1.52) more likely to report using statins than those with a QRISK score <10. Participants reporting using statins had lower mean low-density lipoprotein cholesterol levels (the biological target of statins), compared with non-statin users (Supplementary Figure 3).

Association of education with QRISK3 score and statin use

Per year increase in education was associated with a -0.30 (95% CI: -0.30 to -0.29) reduction in mean QRISK3 score in females and a -0.35 (95% CI: -0.35 to -0.34) reduction in males (Supplementary Table 8 and Supplementary Figure 4).

Statin prevalence was highest in those with ≤7 years of education (equivalent to no formal qualifications) across all strata of cardiovascular risk (Supplementary Figure 5 and Supplementary Table 9). Each additional year of education was associated with a lower odds of statin use (OR in females: 0.93; 95% CI: 0.93 to 0.93; OR in males: 0.96; 95% CI: 0.96 to 0.96) (Supplementary Figure 6).

Interaction between education and QRISK3 score in relation to statin use

There was evidence of an interaction between QRISK3×education on statin use. In females, per unit increase in QRISK3, the OR for reporting statin use in those with ≥20 years (equivalent to obtaining a degree) was 1.14 (95% CI: 1.14 to 1.15) compared with an OR of 1.07 (95% CI: 1.07 to 1.07) for those with ≤7 years of education (Figure 1). In males, the OR for statin use per unit increase in QRISK3 score in those with ≥20 years of education was 1.08 (95% CI: 1.08 to 1.08) compared with an OR of 1.04 (95% CI: 1.04 to 1.05) for those with ≤7 years (Figure 2).

Secondary analyses

There was little evidence of an interaction between QRISK3×education on statin type (Supplementary Table 10 and Supplementary Figure 7).

In analyses in participants with primary care data using i) baseline measures of QRISK3 and self-report statin use, ii) baseline measures of QRISK3 with prescription-validated statin use and iii) QRISK or QRISK2 score recorded in primary care data with a statin prescription, similar interactions were observed to the main results, although evidence of an interaction was weaker in the primary care QRISK analyses in males (Figure 3 and Supplementary Figure 8).

Sensitivity analyses i) using complete case data and ii) excluding participants on non-statin lowering therapy were consistent with the main results (Supplementary Tables 11 and 12).There was evidence of an additive interaction between QRISK3×education , although the strength of the interaction was weaker compared with the multiplicative scale (Supplementary Figure 9).

Pairwise correlation between the baseline derived QRISK3 score and QRISK3 scores derived excluding i) systolic blood pressure variability estimated from the difference between two baseline measures and ii) self-report of any CVD in a mother, father or sibling, were high (all >0.97) (Supplementary Table 13).

Discussion

Despite a higher prevalence of statin use in less educated participants, these participants were less likely to receive statin treatment compared to more highly educated individuals given an equivalent increase in QRISK3 cardiovascular risk score.

Results in context

Cardiovascular risk factors partly mediate the association between education and CVD (2, 19-21) and likely contribute to the greater clinical need for statins in lower educated individuals. However, differences in cardiovascular preventative medication may be further contributing to socioeconomic inequalities. We found the prevalence of statin use in participants at low cardiovascular risk (QRISK3 score of <10%) was similar to previous analyses in UK primary care databases (10). However, notably here, we found the prevalence of statin use in participants with low cardiovascular risk (<10% QRISK3) was higher in participants with lower educational attainment compared with higher educational attainment.

Since 2009, National Health Service (NHS) health checks have been offered to English and Welsh residents aged 40-74 without pre-existing conditions every 5 years, aiming to prevent a number of diseases including CVD (22). A recent systematic review identified seven studies illustrating inequalities in favour of those with higher SEP attending preventative health checks (23), including a trend towards lower uptake in smokers; a socially patterned cardiovascular risk factor (23, 24). Increased engagement with preventative screening may reduce inequalities in CVD and statins. However, in analyses using QRISK scores and statin prescriptions recorded in primary care data, these inequalities remained. Therefore, health-seeking behaviours, including attending primary care clinics, cannot be the sole driver of inequalities.

Previous studies found mixed evidence for the association between SEP and statin use, including the direction of effect (3-8). However, there was often limited consideration for underlying cardiovascular risk (3-6). Forde and colleagues adjusted for Framingham risk score to control for cardiovascular risk (7). In contrast to our results, they found no evidence of inequalities in statin use by strata of employment grade in the Whitehall II study. This difference could be due to different measures of SEP (education vs employment) or cohort differences, where the Whitehall II study is an occupational cohort. The QRISK score has also been shown to have a greater predictive power than the Framingham risk score (25). Therefore, our analyses may better account for cardiovascular risk.

In participants with primary care data, a large number of participants reported taking statins to study nurses but had no prescription at baseline. These Individuals are potentially a combination of those purchasing statins over the counter, having a private prescription, or no longer being prescribed statins. Most individuals (91%) without a linked prescription reported taking Simvastatin (the only statin available over the counter). It is possible that accessing statins through private practices or over the counter are further contributing to inequalities in cardiovascular outcomes.

Strengths and limitations

The major strength of our work is the large sample size and array of data available. Given the age of participants, statin prevalence is high. Using linked primary care data for 44% of the eligible sample we could i) validate self-reported statin use and ii) compare different mechanisms inequalities may arise. Where inequalities are present in primary care QRISK scores, inequalities are potentially due to factors within clinic settings. Using QRISK3 scores derived at baseline, inequalities may be due to differences in health seeking behaviour.

Lifestyle and behavioural characteristics included in the QRISK3 score are likely measured more accurately in UK Biobank compared clinics. However, not all variables, or repeat measurements of

variables specified in the QRISK3 algorithm are available in UK Biobank (11). The QRISK3 algorithm includes medications where an individual has two or more prescriptions for each class of medication (e.g., corticosteroid or atypical antipsychotic). We relied on a single self-report measure at baseline, which may overestimate medication use. However, the magnitude to which these measurements differ is unlikely to introduce much bias to the QRISK3 score. Systolic blood pressure variability and coronary heart disease in a first degree relative under the age of 60, are not available in UK Biobank. Although we have included measures likely to capture some of these variables, this may introduce bias to the QRISK3 estimate.

Participants in UK Biobank are generally of a higher SEP and healthier than the general population, where higher education has been shown to increase participation and socially patterned cardiovascular risk factors including smoking decrease participation (14, 27). Additionally, participants with lower SEP may differ to those of an equivalent SEP (or level of educational attainment) in the general population. Therefore, inequalities in the wider population may be greater than those reported here.

In these data it is not possible to identify who has both received a prescription and subsequently had the prescription filled. E.g., in primary analyses, individuals with the lowest levels of educational attainment may have received a prescription for a statin, but not collected the medication. This may explain why the interaction between QRISK3 scores, and educational attainment is larger in the analyses using self-report statin use compared with statin prescriptions in primary care data.

We have used the ISCED definitions of education as a measure of SEP. Although education is a strong predictor of adulthood SEP, correlating with future employment and income, adult SEP may explain some of the non-linearities observed in these results (28).

Clinical implications

Our results indicate two potential mechanisms for these inequalities. Firstly, there are likely to be differences in health seeking behaviour (29). Secondly, there are important interactions between the healthcare practitioner and patient resulting in unequal prescribing of statins.

Given persisting inequalities in CVD, addressing the contribution of inequalities in statin prescribing provides a clear policy target. However, this requires systemic change and different interventions may be required to address the different mechanisms of inequalities. Future research should investigate the what factors are driving inequalities, such as patient preference for treatment (30) or non up-take of preventative health checks.

Conclusions

Our analyses demonstrate that for a unit increase in cardiovascular risk, individuals with lower levels of education are less likely to be prescribed statins compared with higher educated individuals, meaning differences in statin prescribing likely contribute to inequalities in cardiovascular disease. Policies should consider how these inequalities can be minimised.

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Disclosures

DG is employed part-time by Novo Nordisk. The remaining authors have no conflicts of interest to declare.

Contributions:

ARC designed the study, cleaned and analysed the data, interpreted the results, wrote and revised the manuscript. DG advised on defining medications, interpreted the results and critically reviewed and revised the manuscript. GDS, AET, NMD and LDH all designed the study, interpreted the results, critically reviewed and revised the manuscript and provided supervision for the project. NMD and LDH contributed equally and are joint senior authors on this manuscript. ARC and LDH serve as guarantors of the paper. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Transparency statement:

ARC affirms that the manuscript is an honest, accurate and transparent account of the study being reported and no important aspects of the study have been omitted.

Patient and public involvement:

No patients were directly involved in setting the research question, developing plans for recruitment, design or implementation of this study. No patients were asked to advise on interpretation or writing of the results. There are no specific plans to disseminate the results of the research to study participants, but the UK Biobank disseminates key findings from projects on its website (https://www.ukbiobank.ac.uk/published-papers; https://www.ukbiobank.ac.uk/news/).

References

1. Bajekal M, Scholes S, O'Flaherty M, Raine R, Norman P, Capewell S. Unequal trends in coronary heart disease mortality by socioeconomic circumstances, England 1982-2006: an analytical study. PLoS One. 2013;8(3):e59608.

2. Carter AR, Gill D, Davies NM, Taylor AE, Tillmann T, Vaucher J, et al. Understanding the consequences of education inequality on cardiovascular disease: mendelian randomisation study. BMJ. 2019;365:l1855.

3. Simpson CR, Hannaford PC, Williams D. Evidence for inequalities in the management of coronary heart disease in Scotland. Heart. 2005;91(5):630-4.

4. Ashworth M, Lloyd D, Smith RS, Wagner A, Rowlands G. Social deprivation and statin prescribing: a cross-sectional analysis using data from the new UK general practitioner 'Quality and Outcomes Framework'. J Public Health (Oxf). 2007;29(1):40-7.

5. Forsberg PO, Li X, Sundquist K. Neighborhood socioeconomic characteristics and statin medication in patients with myocardial infarction: a Swedish nationwide follow-up study. BMC Cardiovasc Disord. 2016;16(1):146.

6. Rasmussen JN, Gislason GH, Rasmussen S, Abildstrom SZ, Schramm TK, Kober L, et al. Use of statins and beta-blockers after acute myocardial infarction according to income and education. J Epidemiol Community Health. 2007;61(12):1091-7.

7. Forde I, Chandola T, Raine R, Marmot MG, Kivimaki M. Socioeconomic and ethnic differences in use of lipid-lowering drugs after deregulation of simvastatin in the UK: the Whitehall II prospective cohort study. Atherosclerosis. 2011;215(1):223-8.

8. Wu J, Zhu S, Yao GL, Mohammed MA, Marshall T. Patient factors influencing the prescribing of lipid lowering drugs for primary prevention of cardiovascular disease in UK general practice: a national retrospective cohort study. PLoS One. 2013;8(7):e67611.

9. Campbell K MA, McCartney G, McCullough S (NHS Health Scotland). Who is least likely to attend? An analysis of outpatient appointment 'Did Not Attend' (DNA) data in Scotland. NHS Health Scotland; 2015.

10. van Staa TP, Smeeth L, Ng ES, Goldacre B, Gulliford M. The efficiency of cardiovascular risk assessment: do the right patients get statin treatment? Heart. 2013;99(21):1597-602.

11. Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ. 2017;357:j2099.

12. Cooper A, O'Flynn N, Guideline Development G. Risk assessment and lipid modification for primary and secondary prevention of cardiovascular disease: summary of NICE guidance. BMJ. 2008;336(7655):1246-8.

13. NICE. Cardiovascular risk assessment and lipid modification. www.nice.org.uk/guidance/qs1002015.

14. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, et al. Comparison of Sociodemographic and Health-Related Characteristics of UK Biobank Participants With Those of the General Population. Am J Epidemiol. 2017;186(9):1026-34.

15. Royston P. Multiple Imputation of Missing Values. The Stata Journal. 2004;4(3):227-41.

16. Tilling K, Williamson EJ, Spratt M, Sterne JA, Carpenter JR. Appropriate inclusion of interactions was needed to avoid bias in multiple imputation. J Clin Epidemiol. 2016;80:107-15.

17. Spratt M, Carpenter J, Sterne JA, Carlin JB, Heron J, Henderson J, et al. Strategies for multiple imputation in longitudinal studies. Am J Epidemiol. 2010;172(4):478-87.

18. Insull W, Kafonek S, Goldner D, Zieve F. Comparison of efficacy and safety of atorvastatin (10mg) with simvastatin (10mg) at six weeks. ASSET Investigators. Am J Cardiol. 2001;87(5):554-9.

19. Hossin MZ, Koupil I, Falkstedt D. Early life socioeconomic position and mortality from cardiovascular diseases: an application of causal mediation analysis in the Stockholm Public Health Cohort. BMJ Open. 2019;9(6):e026258.

20. Kershaw KN, Droomers M, Robinson WR, Carnethon MR, Daviglus ML, Monique Verschuren WM. Quantifying the contributions of behavioral and biological risk factors to socioeconomic disparities in coronary heart disease incidence: the MORGEN study. Eur J Epidemiol. 2013;28(10):807-14.

21. Mejean C, Droomers M, van der Schouw YT, Sluijs I, Czernichow S, Grobbee DE, et al. The contribution of diet and lifestyle to socioeconomic inequalities in cardiovascular morbidity and mortality. International Journal of Cardiology. 2013;168(6):5190-5.

22. England PH. Using the world leading NHS Health Check programme to prevent CVD https://www.gov.uk/government/publications/using-the-nhs-health-check-programme-to-prevent-cvd/using-the-world-leading-nhs-health-check-programme-to-prevent-cvd2018 [updated 24/01/2018. Available from: https://www.gov.uk/government/publications/using-the-nhs-health-check-programme-to-prevent-cvd/using-the-world-leading-nhs-health-check-programme-to-prevent-cvd.

23. Bunten A, Porter L, Gold N, Bogle V. A systematic review of factors influencing NHS health check uptake: invitation methods, patient characteristics, and the impact of interventions. BMC Public Health. 2020;20(1):93.

24. Dalton AR, Bottle A, Okoro C, Majeed A, Millett C. Uptake of the NHS Health Checks programme in a deprived, culturally diverse setting: cross-sectional study. J Public Health (Oxf). 2011;33(3):422-9.

25. Collins GS, Altman DG. An independent external validation and evaluation of QRISK cardiovascular risk prediction: a prospective open cohort study. BMJ. 2009;339:b2584.

26. Finnikin S, Ryan R, Marshall T. Statin initiations and QRISK2 scoring in UK general practice: a THIN database study. Br J Gen Pract. 2017;67(665):e881-e7.

27. Tyrrell J, Zheng J, Beaumont R, Hinton K, Richardson TG, Wood AR, et al. Genetic predictors of participation in optional components of UK Biobank. bioRxiv. 2020:2020.02.10.941328.

28. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 1). J Epidemiol Community Health. 2006;60(1):7-12.

29. Cookson R, Propper C, Asaria M, Raine R. Socio-Economic Inequalities in Health Care in England. Fisc Stud. 2016;37(3-4):371-403.

30. Schroder SL, Fink A, Richter M. Socioeconomic differences in experiences with treatment of coronary heart disease: a qualitative study from the perspective of elderly patients. BMJ Open. 2018;8(11):e024151.

Figures

Figure 1: Study flow chart identifying eligible participants for analysis

Figure 2: Odd ratio for self-report statin use per unit increase in baseline QRISK3 score with no education interaction and stratified by years of education in females and males, adjusted for date of baseline assessment centre

Analyses stratified by years of education provide an estimate of interaction on the multiplicative scale. P value for interaction in females = $1.896x10^{-85}$ and males = $1.999x10^{-48}$

Figure 3: Odd ratio for statin use recorded in primary care prescription data per unit increase in A) baseline QRISK3 score and B) QRISK or QRISK2 score recorded in primary care, in females and males adjusted for date of baseline assessment centre or date of QRISK assessment in primary care

Analyses stratified by years of education provide an estimate of interaction on the multiplicative scale.

Baseline QRISK3: P value for interaction in females =$5.476 x10^{-10}$ and males = $4.046x10^{-7}$

QRISK score recorded in primary care: P value for interaction in females = 0.006 and males = 0.413